ENVIRONMENTAL TOBACCO SMOKE AND LUNG CANCER: AN EVALUATION OF THE RISK

EXECUTIVE SUMMARY

Scope of the Report

This report addresses the possible association between exposure to environmental tobacco smoke (ETS) and lung cancer in non-smokers. To investigate this issue in a thorough and professional manner, we have reviewed the scientific literature and brought our own scientific experience to bear on the problem. The expertise within this group is of direct relevance to the process of carcinogenesis, spanning molecular, genetic, biochemical, nutritional, statistical and clinical areas. The entire report can be viewed as a risk assessment, combining the analysis of hazard identification, exposure assessment, statistical associations and biological endpoint evaluation. The report of this independent Working Group is intended to add to the debate, in the hope that it will stimulate further research in this important area of science.

Main Conclusions:

chemical composition

ETS cannot be equated with mainstream or sidestream tobacco smoke. In fact, in every-day settings where ETS has actually been measured, only a few of the many compounds present in tobacco smoke have been detected. In order to allow some calculation of exposure level, a model was developed and calculated concentrations of putative ETS components were derived. This model showed that the concentration of the likely chemical constituents of ETS is 10 to 1,000,000 times lower than permitted levels of exposure in the workplace.

statistical associations

The 48 epidemiological studies concerning ETS exposure that have been performed to date are extremely variable in quality and in the associations they report. A homogeneous sub-group of 20 studies have considered exposure in the workplace. If the relative risk (RR) values from these workplace studies are combined using estimation meta-analysis, a pooled estimate of 1.04 (95% confidence limits [CL]: 0.95-1.14) is obtained, which is not significantly different from a zero increase in risk. Similarly, if the US workplace results, which are the largest number of studies for a single nation, are combined a pooled estimate of 1.02 (95%CL: 0.93-1.13) is obtained.

Lung cancer is a disease with a latency counted in decades rather than years. This suggests that, if ETS causes lung cancer, it may be more readily detected from childhood rather than from adult exposure. The overall findings of the 17 studies in which childhood exposure was questioned were not different from a zero increase in risk, even if the exposure measure with the largest RR in each study is chosen for pooling.

Forty-three studies have considered the association between a husband's smoking and his wife's incidence of lung cancer (female studies) but only nine have considered the reverse (male studies). One study reports joint male/female results. Analysis shows that the studies are heterogeneous and so they cannot be considered as a single group. The 16 US studies comprise the largest national database both in the number of studies and the total number of lung cancer cases investigated. The major bias apparent in the US studies is that of smoker misclassification, which can produce a spurious association between spousal smoking and lung cancer. The presence of this bias has been generally accepted but its magnitude has been the subject of some debate. Using conservative assumptions, an overall smoker misclassification bias estimate for the US studies would be 1.14. Correction of the US results for misclassification bias yields a risk estimate of 1.01 (95%CL: 0.90-1.13), a result not significantly different from a zero increase in risk.

The epidemiological studies investigating an association between ETS exposure and lung cancer are at, and many would say beyond, the limits of epidemiological science. After all Breslow and Day, in their standard reference book, stated that relative risks "of less than 2.0 may readily reflect some unperceived bias or confounding factor, those over 5.0 are unlikely to do so". It should be no surprise, therefore, that the spousal smoking study results are erratic and contradictory.

lifestyle biases

It is now widely accepted that diet is related to approximately one-third of all human cancers. This observation is particularly relevant to lung cancer because it is recognised as being amongst the most sensitive of tumours related to diet, being inversely correlated with intake of fruits and vegetables in some 30 epidemiological studies. Further, as opposed to protection afforded by consumption of higher amounts of fruits and vegetables, a diet rich in saturated fat is a positive modulator, leading to a higher incidence and a shorter latency period for the development of lung cancer, especially adenocarcinoma.

It is also important to emphasise that various food products often contain many of the chemicals reported to be present in ETS, and that the amounts of these chemicals in the daily diet usually exceed by far what might be taken up by breathing indoor air. For some compounds, daily dietary intake exceeds intake from any possible inhalation source by one thousand fold.

Evidence is accumulating that having a smoking spouse is associated with a vast range of lifestyle, personality and occupational factors other than diet, many of which are strong candidates as risk factors for lung cancer. Significant differences both in lifestyles and socio-psychological behaviours among the nonsmokers living with smokers compared to those living with nonsmokers certainly strengthens that conclusion. Exposure to ETS is unlikely to be a significant risk factor for lung cancer in humans (particularly women married to smokers) because, compared to such a low-level of exposure to chemicals, other common lifestyle risk factors are likely to play more significant roles.

defence mechanisms

The body has many defence mechanisms that protect against the development of cancer. These include metabolic detoxication, immune surveillance and DNA repair. Any putative mechanism for the development of lung cancer following exposure to ETS must involve some consideration of possible DNA damage. Two factors are important in this respect. First of all, ETS-related DNA damage has to occur at the target organ (i.e., lung tissue) in order to be related to the adverse biological effect of concern. There is insufficient evidence that exposure to ETS leads to DNA damage in lung tissue. This is especially true in comparison to DNA damage induced by other airborne environmental exposures or endogenously induced DNA damage. Second, the possible role of DNA repair in the aetiology of lung cancer should be considered. It is now clear that some common forms of cancer are associated with suboptimal or deficient DNA repair. Recent studies suggest that some types of DNA repair are deficient in otherwise-normal patients with hereditary nonpolypous colon cancer. Animal experiments have also demonstrated that improved DNA repair protects against cancer. Thus, processes like DNA repair are likely to play a key role in the human interaction with the internal environment and, indeed, may introduce a threshold below which a chemical exposure poses no risk to humans. Although the pathway from DNA damage to mutations and onwards to tumours is by no means fully understood, for the purposes of risk assessment a linear dose response relationship cannot be assumed. For many reasons this would appear to be the least likely possibility because, for example, chemical carcinogenesis is a well-recognised multi-stage process which cannot, therefore, follow first order kinetics.

risk assessment

As stated above, this entire report represents a risk assessment of ETS exposure. Often, an unfounded assumption regarding the similarity between ETS and either mainstream or sidestream tobacco smoke is used to justify an argument of biological plausibility. This report suggests that such an assumption is inappropriate. The current documentation of the minimal contribution of ETS to chemicals to the indoor environment, the heterogeneous and inconsistent quality of the epidemiological studies in this area, the ubiquitous nature of normal, everyday chemical exposures, for example from dietary sources, and the presence of defence mechanisms, such as chemical detoxication and DNA repair, suggest that it is beyond the limits of current science to conclude that ETS exposure significantly adds to the risk of human lung cancer. It is the overall evaluation of the Working Group that there exists insufficient evidence to endorse the view that ETS is a primary lung carcinogen.